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| 26158 7590 07/02/2008<br>WOMBLE CARLYLE SANDRIDGE & RICE, PLLC<br>ATTN: PATENT DOCKETING 32ND FLOOR<br>P.O. BOX 7037<br>ATLANTA, GA 30357-0037 |             |                      |                     |                  |
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| KOSAR, AARON J   |             |                      |                     |                  |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/524,318

**Applicant(s)**

BOURGEOIS ET AL.

**Examiner**

AARON J. KOSAR

**Art Unit**

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 February 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 12-60 and 62-65 is/are pending in the application.
- 4a) Of the above claim(s) 19-27, 37-44, 56-58 and 66-69 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12-18, 28-36, 45-55, 59, 60 and 62-65 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 3/3/08, 3/10/08
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's amendment and argument filed 27 February 2008 in response to the non-final rejection are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Applicant has amended the claims by canceling claim 61. Claims 12-60 and 62-69 are pending, of which claims 19-27, 37-44, 56-58, and 66-69 are withdrawn claims. Claims 12-18, 28-36, 45-55, 59, 60, and 62-65 are pending and have been examined on the merits to the extent of the elected invention.

### ***Claim Rejections - 35 USC § 112***

#### **The following is a quotation of the first paragraph of 35 U.S.C. 112:**

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Claim 65** is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has reasonably demonstrated/disclosed that the claimed compound is useful as a therapeutic agent for treating symptoms of the exemplified inflammatory bowel disease (IBDs); however, the claims also encompass using the claimed compound to have specificity towards treating colitis and Crohn's disease which is clearly beyond the scope of the instantly disclosed/claimed invention. Please note that specificity towards treating Crohn's disease/ulcerative colitis requires a higher standard for enablement than does treating the

symptoms of these disorders, especially since the disorders themselves cannot be totally prevented with current therapies, are incurable, and the causative agents are not yet understood/determined (e.g. see C:PTO-892 8/24/2007 - USPATENT APPLICATION 10/347,877,column 1, ¶1,5,and 6 (*cf.* issued as US 7,018,629 B2)).

### ***Response to Arguments***

Applicant has argued that treatment of the subspecies of ulcerative colitis is known. Applicant's arguments have been fully considered, but respectfully, they have been found to be not persuasive. The arguments are not persuasive because Applicant has not traversed the objective evidence of record (C:PTO-892 8/24/2007), the species of Crohn's disease or colitis, and has referred to potential references which have not been made of record. The arguments of counsel cannot take the place of the evidence in the record. Therefore, the ground of rejection is maintained.

#### **The following is a quotation of the second paragraph of 35 U.S.C. 112:**

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 12-18, 28-36, 45-55, 59, 60, and 62-65** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In general, it is clear that a device (an apparatus, (I)) can consist of the device itself ((I): "(b) a drug delivery device"); however, it is unclear how a device (I) may comprise the device itself (I', where I=I') and also a second/additional component ((II'): (a) an active agent/composition of matter) (such that effectively  $I = I + II'$ ). It is unclear if the invention comprises more than one device.

Furthermore, the claims are drawn to an *apparatus* (a drug delivery device), which is of a different statutory classification of invention than a *composition of matter* (e.g. active agents, chemical compositions/components), thus two invention classifications are proposed single claims though the claims are required to claim only one (class of) invention per claim. One of skill would not be apprised as to the subject matter embraced by the claims and would not be able to determine the metes and bounds of the claims, rendering the claims indefinite.

Please note, however, this ground of objection may be overcome, for example, by amending the claims to recite the device (or composition) (I) correlated to and clearly distinguished from the respective component devices (or component compositions) ((I'),(II')): such that  $I=I'+II'$  and  $I \geq I'$  comprising device/composition (I).

The term "isolated" recited in claims 12, 28, 35, 45, and 59 is a relative term which renders the claims indefinite. The term "isolated" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Absent objective criteria by which the degree of isolation is determined (e.g. identification of structural/compositional elements and proportions or quantities thereof enriched/removed/isolated or a reference point by which the degree of isolation may be ascertained), the instant claims are thus still deemed to be anticipated by/ made obvious over the compositions made of record.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The claims are generally drawn to an apparatus, in particular a drug-delivery device.

It is further noted that the apparatus claims state an intended operation (*e.g.* see claim 12, oral administration and colonic release) and/or the contents during the intended operation (active agent); however as stated in MPEP § 2114 “apparatus claims cover what a device *is*, not what a device does” (*Hewlett-Packard Co. vs. Bausch and Lomb, Inc.*, 909 F.2d 1464, 1469, 15 USPQ2d 1525, 1528 (Fed.Cir.1990).

Also, the drug delivery device/apparatus is not reliant on the contents of the apparatus (*e.g.* the pharmaceutical composition/active agent). MPEP § 2115 states, “Expressions relating the apparatus to contents thereof during an intended operation are of no significance in determining patentability of the apparatus claim.” *Ex parte Thibault*, 164 USPQ 666, 667 (Bd. App. 1969). Furthermore, “[i]nclusion of material or article worked upon by a structure being claimed does not impart patentability to the claims.” *In re Young*, 75 F.2d 996, 25 USPQ 69 (CCPA 1935) (as restated in *In re Otto*, 312 F.2d 937, 136 USPQ 458, 459 (CCPA 1963)).

Though the patentable weight relies upon the device (apparatus). The composition that has also been disclosed has also been considered with respect to the teachings of the prior art, and for the sake of compact prosecution, the rejection under 35 U.S.C. 102(b) below is drawn to the extent of the composition most closely related to the limitations of the apparatus claims.

**Claims 12-14, 28-31, 36, 59, 60, and 62, and 65** are rejected under 35 U.S.C. 102(b) as being anticipated by OLSHENITSKY (US 6,500,423) as evidenced by ARTHUR (Arthur, M. et al. Annales de l'institut Pasteur, Microbiologie. 137(1.1) Jan/Feb 1986, pages 125-134.) and OUNISSI (Ounissi, H. and Courvalin, P. Gene.1985, 35(3), pages 271-278.).

Olshenitsky teaches a composition comprising an active agent and a drug delivery device. Olshenitsky teaches the drug delivery device suitable for administering the active agent to the colon in teaching an oral/flavor-enhanced probiotic composition for treating the gastrointestinal (GI) tract (Summary ¶1-3, columns 3 and 4). Though Applicant fails to claim the object/subject receiving the drug delivery device, Olshenitsky discloses a device treating a human, and a variety of mammals and avians (column 3, lines 29-44). Olshenitsky also teaches that *Escherichia coli* (and/or the probiotic composition comprising *E. coli*), for example as a food additive or with a flavouring agent (an oral composition), carries the probiotic effect into the GI tract. Olshenitsky further teaches that for conditions treated by antibiotics, probiotics enable the host's gut microflora to return to normal levels (column 1, lines 56-64).

As evidenced by Arthur and Ounissi, *E. coli* and a variety of organisms inherently contain/produce erythromycin esterase (Abstracts). Thus administering *E.coli* orally to the gut necessarily provides delivery of erythromycin esterase (drug/active agent) to the same GI environment via the bacterial organism (drug delivery device).

With respect to claims 36 and 59, the bacteria and products produced therein anticipates: an antibiotic (*E.coli* competes against other GI microbes); anti-inflammatory (the composition treats IBDs); and a peptide/protein/gene/anti-sense oligonucleotide/diagnostic agent/bacteria (*E. coli*, it's structural components, and produced molecules).

***Response to Arguments***

Applicant has argued that the prior art does not teach the amendment of isolated enzymes (Remarks, page 14). Applicants arguments have been fully considered, but found to be not persuasive, because the apparatus/device comprising the device of (b) is not further limited by the further limitations of the contents of (a) (MPEP § 2114 and 2115) or in the alternative, are still deemed to be anticipated by the prior art (see 35 USC 112, 2<sup>nd</sup> ¶, *supra*), and thus the rejection, for the reasons of record is maintained.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 12-18, 28-36, 45-55, 59, 60, and 62-65** are rejected under 35 U.S.C. 103(a) as being unpatentable over SRIAMORANSACK (GG: PTO-1449), MUNJERI (U, PTO-892: Munjeri, O., *et al.* Journal of Pharmaceutical Sciences. 1998, 87(8), 905-908.), NOGUCHI (Noguchi, N., *et al.* J. Bacteriology. 2000, 182(18), 5052-8). and OUNISSI (Ounissi, H. and

Courvalin, P. Gene.1985, 35(3), 271-278). Sriamorsak and Munjeri (U) teach an active agent, a pectinate bead, which is suitable for colonic release of a variety compounds, including release of protein. Noguci and Ouinissi teach proteins, including isolates of the enzymes erythromycin esterase and macrolide 2'-phosphotransferase I (Mph(A), which are capable of inactivating antibiotics and which are produced by/isolated from a resident microorganisms native to GI tract flora (including the colon).

Both the active agent and the carrier were known in art. The only difference is the combination of "old elements" into a single composition by enclosing the enzyme with the pectinate bead.

Thus it would have been obvious to one having ordinary skill in the art to admix the pectinate and enzyme, since the *delivery agent* of the active agent is not dependent upon the active agent (the pectinate appears to be generic to the delivery of any compound to the colon, and because the functioning of the active agent is not dependent upon the delivery agent (i.e. the delivery agent appears to only interdigitate with the carrier, but does not affect the function of or otherwise interact with the active agent). Furthermore, the combination of a pectinate with a protein such as erythromycin esterase would have yielded predictable results to a person of ordinary skill in the art at the time of the invention (a composition suitable for delivery to the colon using (a) a colonic delivery pectinate and (b) a protein indigenous to the colon as argued above).

### **Response to Arguments**

Applicant has argued that it would not be obvious to administer the enzymes to the colon, as required by the claims. Applicant's arguments have been fully considered; however,

respectfully, they are not persuasive. In response to applicant's argument, a chemical composition and its properties are inseparable (MPEP §2112.01). Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition(s) of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product(s) of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the arguments of record and the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at

Art Unit: 1651

the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### ***Conclusion***

The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure.  
BOUMEESTERS, J.F., et al (USPATENT 6,436,461 as evidenced by WO 98/15192) *teaches gel compositions comprising calcium pectinate; the advantages of derivatizing (partially esterified); reticulating a multivalent cation; and using at least one active ingredient (various, Abstract; page 11, ¶ 2; Example 14, figure and lines 12-15).*

MATHOWITZ, E. (Mathiowitz, E. "Oral Drug delivery, Small Intestine & Colon", Encyclopedia of Controlled Drug Delivery, Volumes 1-2. 1999, pages 717-728.) *teaches colonic delivery compositions, including pectinate or calcium pectinate (CaP) compositions (e.g. page ¶4 and table 3, page 723; page 724). Mathowitz also teaches the benefit of colonic enzymes in promoting colonic release treatments, teaching that all individuals have very high resident populations of bacteria in the ascending colon, and this ubiquitous presence can justify efforts to target these bacterial enzymes as potential triggers for controlled-release technology" (page 721, lines 10-12). [Please note, for the sake of compact prosecution, the best available copy of this reference has been provided herewith; however, a clean copy shall be provided when the reference becomes available to the Examiner.]*

LEONARD, F., et al (Leonard F., et al., "Use of Beta-Lactamase-producing Anaerobes to prevent Ceftriaxone from Degrading Intestinal Resistance to Colonization" J. Infectious Disease. 1989, 160(2), 274-280 (CAS ABSTRACT).) *teaches treating an antibiotic-enriched and beta-lactamase deficient mammal (ceftriaxone/beta-lactamase/mouse) with a beta-lactamase delivery vehicle (beta-lactamase producing anaerobes). Leonard teaches the composition is provided orally and that the treatment provides resistance to C.albicans and E.cloacae as measured by fecal flora. This constitutes a teaching of delivering an effective amount of beta-lactamase enzyme/enzyme-producing bacteria throughout the lower GI tract/colon for the purpose of reducing colonic antibiotic concentrations.*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AARON J. KOSAR whose telephone number is (571)270-3054. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Aaron J Kosar/  
Examiner, Art Unit 1651

/Sandra Saucier/  
Primary Examiner, Art Unit 1651